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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/832,899	04/12/2001	Jean-Marc Balloul	032751-052	1686

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EXAMINER	
BROWN, TIMOTHY M	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 01/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/832,899	BALLOUL ET AL.	
	Examiner	Art Unit	
	Timothy M. Brown	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-7 and 10-25* is/are pending in the application.

4a) Of the above claim(s) *7,16,17 and 19-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,10-12,18 and 25* is/are rejected.

7)☒ Claim(s) *3,6,13-15 and 24* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Final Office Action is responsive to the communication received November 18, 2005. Claims 1-3, 5, 6, 10-15, 18, 24 and 25 are under examination. Claims 7, 16, 17 and 19-23 are withdrawn.

Claim Objections

Claims 3, 6, 13-15 and 24 are objected to for depending from a rejected base claim. These claims would be allowable if presented in independent form.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 is indefinite in the recitation of "a cellular protein differentially or overexpressed" on tumor cells. It is unclear how a cellular protein that is "differentially" or "overexpressed" may serve as an anti-ligand for targeting tumor cells when normal cells would also express the cellular protein, albeit at different levels. Thus, directing infection using such proteins would not "target" the poxviral particle to the target cell. "Differentially" and "overexpressed" are also terms of degree that lack adequate clarification in the specification. The specification fails to provide endpoints for these relative terms that would allow one skilled in the art to appreciate the scope of the claimed invention. Amending the claims to provide that

the "differentially or overexpressed" polypeptides comprise the polypeptide examples referred to in Applicants' traverse would overcome this rejection.

Claim 5 is further indefinite in the recitation of "certain angiogenic growth factors." It is unclear how "certain" modifies the angiogenic growth factors claimed. Thus, one skilled in the art would not be able to determine the metes and bounds of the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 5 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. Although the specification enables targeting poxviral particles using cellular antigens that are overexpressed on tumor cells, the specification does not enable targeting poxviral particles using cellular antigens that are "differentially expressed" on tumor cells. Making and using such a poxviral particle would require one of ordinary skill in the art to invest undue experimentation.

A number of factors are considered in determining whether "undue experimentation" is required. These factors include: the breadth of the claims; the nature of the invention; the state of the prior art; the level of one of ordinary skill; the level of predictability in the art; the amount of direction provided by the inventor; the existence of working examples; and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404.

In this case, claim 5 provides that poxviral particle is targeted based on a cellular antigen that is differentially expressed on tumor cells. Giving the claims their broadest reasonable

interpretation, "differentially expressed" implies that the tumor-specific antigen may be underexpressed in tumor cells. Although targeting viral infection to tumor cells has been practiced in the art, it typically involves using cellular antigens that are expressed in greater numbers on tumor cells than on normal cells (see e.g. Cancer Gene Therapy (2000) 7, 6, 901-904). One skilled in the art could not predict how to target viral infection based on cellular antigens that are underexpressed on tumor cells since these tumor cells would not bind and integrate virus. Thus, practicing the claimed invention would require one skilled in the art to rely heavily on the guidance of Applicants' specification. The content of the specification however relates to cellular antigens that are overexpressed on tumor cells (see e.g. specification, p. 10). Based on the lack of guidance in the specification and the unpredictability of targeting viral infection using underexpressed cellular antigens, one skilled in the art would have to invest undue experimentation in order to make and use the invention as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 2, 10-12, 18 and 25 rejected under 35 U.S.C. 102(a) as being anticipated by Collado et al. (Vaccine (July 2000) 18, 3123-3133).

Applicants' claims are interpreted as being drawn to a poxviral particle having a targeted infection specificity that is provided by a heterologous targeting ligand, wherein the heterologous

targeting ligand is a polypeptide that is fused to the expression product of the A27L gene (i.e. p14), and wherein the poxviral particle is an intracellular mature virus (IMV). The claims provide that the ligand is fused to the N-terminus of p14 and that the ligand further comprises a signal peptide.

Collado et al. disclose a recombinant vaccinia virus having a heterologous p14 polypeptide comprising p14 fused to the Env protein of HIV (see e.g. abstract, lines 3-5). Collado et al. provide that the heterologous polypeptide is fused to the N-terminus of p14 (Fig. 1) and that the heterologous polypeptide comprises a trans-Golgi signal peptide. It follows that the heterologous polypeptide has a trans-Golgi signal peptide in that the heterologous polypeptide is glycosylated during the post-translational processing of the heterologous polypeptide in BCS-40 cells (see p. 3126). Based on this disclosure, Collado et al. anticipate the subject matter of claims 1, 2, 10-12, 18 and 25.

Response to Arguments

35 U.S.C. 112, second paragraph

Claim 1 was rejected as indefinite because the language "wherein said ligand moiety is a polypeptide" lacked antecedent basis. This rejection has been withdrawn in view of Applicants' amendment.

Claim 5 was rejected because the language "differentially" and "overexpressed" presents relative terminology. This rejection is maintained. Although not indefinite *per se*, relative terms must have some standard in the specification for defining their degree. In the absence of such a standard, it must be determined whether one skilled in the art would nevertheless be reasonably

apprised of the scope of the invention. See *In re Wiggins*, 488 F. 2d 538, 541, 179 USPQ 421, 423 (CCPA 1973). Here, Applicants' specification fails to disclose a standard that would allow the skilled artisan to determine whether a selected protein is expressed differentially or overexpressed. The status of the art is no less helpful since it is not clear what values "differentially" and "overexpressed" are relative to. One skilled in the art would not know what expression levels are encompassed by thislanguage.

Note that amending claim 5 to recite specific cellular proteins does not overcome the rejection. Although it is clear which proteins claim 5 refers to, it remains unclear what expression values qualify as 'differential' or 'overexpression.' That is, the skilled artisan must still evaluate whether the claimed cellular protein (e.g. TNF receptor) is "differentially" or "overexpressed."

35 U.S.C. 112, first paragraph

The enablement rejection of claim 5 is maintained. Claim 5 is not enabled because it would require undue experimentation to target a poxviral particle to a cellular protein that is differentially (i.e. sparsely) expressed. Amending the claims to require a specific cellular protein does not overcome this rejection because the claims require targeting specific cell-surface ligands that are differentially (i.e. sparsely) expressed. Sparsely expressed ligands cannot be used to target poxvirus for the reasons discussed above.

35 U.S.C. 102

The rejection of claims 1, 2, 10-12, 18 and 25 under 35 U.S.C. 102(a) is maintained. Applicants traverse the rejection based on a priority claim to European Patent Applications 00440109.7 and 01440009.7. Applicant cannot rely upon the foreign priority papers to

overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy M. Brown whose telephone number is (571) 272-0773. The examiner can normally be reached on Monday - Friday, 8am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Timothy M. Brown
Examiner
Art Unit 1648

tmb

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